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Research

Formulation and evaluation of piroxicam mucoadhesive buccal tablets

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Abstract

Mucoadhesive tablets of Piroxicam were prepared by using Tragacanth, Xanthan gum and Tamarind Gum as mucoadhesive polymers. Nine formulations were developed with varying concentrations of polymers. F1 to F9 formulations were composed of Tragacanth, Xanthan gum and Tamarind Gum in ratios of 1:1, 1:2 and 1:3. The formulated mucoadhesive buccal tablets were assessed for quality attributes like weight variation, hardness, thickness, friability, drug content, moisture absorption, surface pH and *in vitro* drug release studies. Optimized formulation G4 showed maximum release of the drug (99.61%). The FTIR results showed no evidence of interaction between the drug and polymers. All the evaluation parameters given the positive result and comply with the standards. The results indicated that the mucoadhesive buccal tablets of Piroxicam may be good choice to bypass the extensive hepatic first pass metabolism with an improvement in bioavailability of Piroxicam through buccal mucosa.

Keywords: Piroxicam, Tragacanth, Xanthan gum, Tamarind Gum and Buccal tablets.

INTRODUCTION

Buccal delivery of drugs provides an attractive alternative to the oral route of drug administration, particularly in overcoming deficiencies associated with the latter mode of dosing .Problems such as first pass metabolism and drug degradation in the GIT environment can be circumvented by administering the drug via buccal route. Moreover, the oral cavity is easily accessible for self medication and be promptly terminated in case of toxicity by removing the dosage form from buccal cavity. It is also possible to administer drugs to patients who cannot be dosed orally via this route Successful buccal drug delivery using buccal adhesive system requires at least three of the following (a) A bioadhesive to retain the system in the oral cavity and maximize the intimacy of contact with mucosa (b) A vehicle the release the drug at an appropriate rate under the conditions prevailing in the mouth and (c) Strategies for overcoming the low permeability of the oral mucosa. Buccal adhesive drug delivery stem promote the residence time and act as controlled release dosage forms.

The use of many hydrophilic macromolecular drugs as potential therapeutic agents is their in adequate and erratic oral absorption. However, therapeutic potential of these compounds lies in our ability to design and achieve

effective and stable delivery systems. Based on our current understanding, it can be said that many drugs cannot be delivered effectively through the conventional oral route.

The main reasons for the poor bio-availability of many drugs through conventional oral route are:

- ✓ Pre-systemic clearance of drugs.
- ✓ The sensitivity of drugs to the gastric acidic environment which leads to gastric irritation. Limitations associated with gastro intestinal tract like variable absorption characteristics.

Buccal mucosa composed of several layers of different cells. The Epithelium is similar to stratified squamous epithelia found in rest of the at least one of which is biological nature are held together by means of interfacial forces.[1]

Buccal drug delivery is a type of bioadhesive drug delivery especially it is a mucoadhesive drug delivery system is adhered to buccal mucosa.

- ➢ The term bioadhesion is commonly defined as an adhesion between two materials where at least one of the materials is of biological origin. In the case of bioadhesive drug delivery systems, bioadhesion often refers to the adhesion between the excipients of the formulation (i.e. the inactive media) and the biological tissue.
- ➢ The term mucoadhesion can be considered to refer to a sub group of bioadhesion and, more specifically, to the case when the formulation interacts with the mucous layer that covers a mucosal tissue.

The mucosal layer lines a number of regions of the body including gastrointestinal tract, urogenital tract, airway, ear, nose and eye. Hence mucoadhesive drug delivery system includes the following.

1. Buccal delivery system
2. oral delivery system
3. Ocular delivery system
4. Vaginal delivery system
5. Rectal delivery system
6. Nasal delivery system[2]

Overview of the Oral Mucosa Structure The oral mucosa is composed of an outermost layer of stratified squamous epithelium. Below this lies a basement membrane, a lamina propria followed by the submucosa as the innermost layer18, 19 can be seen in figure 1. The epithelium of the buccal mucosa is about 40- 50 cell layers thick, while that of the sublingual epithelium contains somewhat fewer. The epithelial cells increase in size and become flatter as they travel from the basal layers to the superficial layers. The turnover time for the buccal epithelium has been estimated at 5-6 days[3], and this is probably representative of the oral mucosa as a whole. The oral mucosal thickness varies depending on the site: the buccal mucosa measures at 500-800 µm, while the mucosal thickness of the hard and soft palates, the floor of the mouth, the ventral tongue, and the gingivae measure at about 100-200 µm. The composition of the epithelium also varies depending on the site in the oral cavity. The mucosae of areas subject to mechanical stress (the gingivae and hard palate) are keratinized similar to the epidermis. The mucosae of the soft palate, the sublingual, and the buccal regions, however, are not keratinized[4]. The keratinized epithelia contain neutral lipids like ceramides and acylceramides which have been associated with the barrier function. These epithelia are relatively impermeable to water. In contrast, nonkeratinized epithelia, such as the floor of the mouth and the buccal epithelia, do not contain acylceramides and only have small amounts of ceramide [5-7]. They also contain small amounts of neutral but polar lipids, mainly cholesterol sulfate and glucosyl ceramides. These epithelia have been found to be considerably more permeable to water than keratinized epithelia.

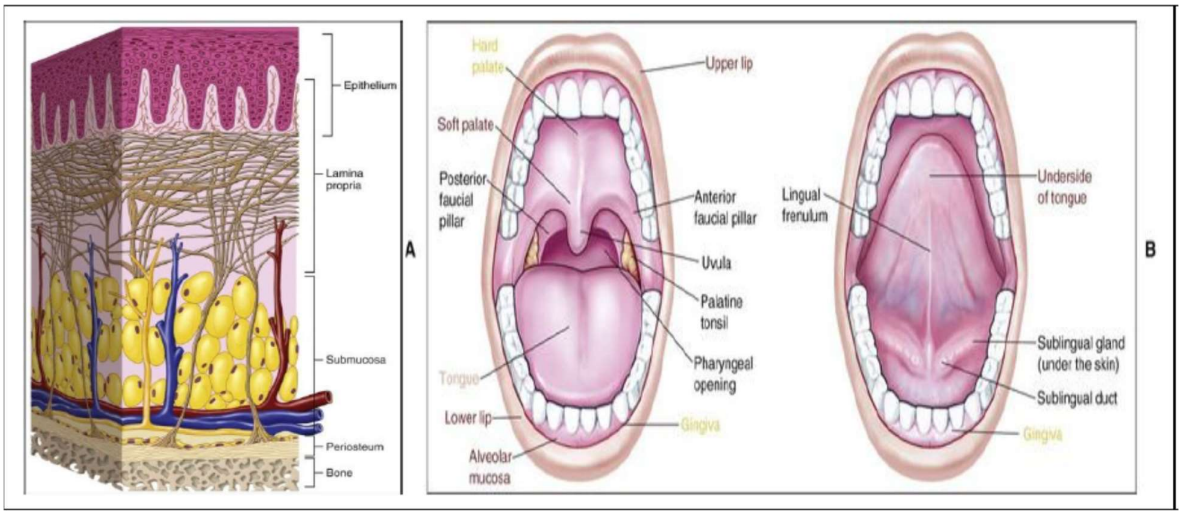

Fig 1: Anatomy of Oral Mucosa

Permeability

The oral mucosa in general is somewhat leaky epithelia intermediate between that of the epidermis and intestinal mucosa. It is estimated that the permeability of the buccal mucosa is 4-4000 times greater than that of the skin[8]. As indicative by the wide range in this reported value, there are considerable differences in permeability between different regions of the oral cavity because of the diverse structures and functions of the different oral mucosae. In general, the permeabilities of the oral mucosae decrease in the order of sublingual greater than buccal, and buccal greater than palatal. This rank order is based on the relative thickness and degree of keratinization of these tissues, with the sublingual mucosa being relatively thin and non-keratinized, the buccal thicker and non-keratinized, and the palatal intermediate in thickness but keratinized.

Environment

The cells of the oral epithelia are surrounded by an intercellular ground substance, mucus, the principle components of which are complexes made up of proteins and carbohydrates. These complexes may be free of association or some maybe attached to certain regions on the cell surfaces. This matrix may actually play a role in cell-cell adhesion, as well as acting as a lubricant, allowing cells to move relative to one another[9]. Along the same lines, the mucus is also believed to play a role in bioadhesion of mucoadhesive drug delivery systems.

Ideal Characteristics of Buccal Drug Delivery System[10]

- ✓ Should adhere to the site of attachment for a few hours.
- ✓ Should release the drug in a controlled fashion.
- ✓ Should provide drug release in a unidirectional way toward the mucosa.
- ✓ Should facilitate the rate and extent of drug absorption.
- ✓ Should not cause any irritation or inconvenience to the patient.
- ✓ Should not interfere with the normal functions such as talking and drinking.

Mechanism of mucoadhasive

Several theories have been put forward to explain the mechanism of polymer–mucus interactions that lead to mucoadhesion. To start with, the sequential events that occur during bioadhesion include an intimate contact between the bioadhesive polymer and the biological tissue due to proper wetting of the bioadhesive surface and swelling of the bioadhesive. Following this is the penetration of the bioadhesive into the tissue crevices, interpenetration between the mucoadhesive polymer chains and those of the mucus. Subsequently low chemical bonds can become operative. Hydration of the polymer plays a very important role in bioadhesion. There is a critical degree of hydration required for optimum bioadhesion. If there is incomplete hydration, the active adhesion sites are not completely liberated and available for interaction. On the other hand, an excessive amount of water weakens the adhesive bond as a result of an overextension of the hydrogen bonds. During hydration; there is a dissociation of hydrogen bonds of the polymer chains. The polymer–water interaction becomes greater than the polymer-polymer interaction, thereby making the polymer chains available for mucus penetration. Following polymer hydration intermingling between chain segments of the mucoadhesive polymer with the mucus occurs. The factors critical for this model of mucoadhesion are the diffusion coefficient of the polymer, contact time and contact pressure. The polymer diffusion coefficient is influenced by the molecular mass between cross-links, and is inversely related to the cross-linking density.[11-14]

Advantages of buccal drug delivery system

1) Bypass the gastrointestinal tract and hepatic portal system, increasing the bioavailability of orally administered drugs that otherwise undergo hepatic first-pass metabolism. In addition the drug is protected from degradation due to pH and digestive enzymes of the middle gastrointestinal tract.
2) Improved patient compliance due to the elimination of associated pain with injections; administration of drugs in unconscious or incapacitated patients; convenience of administration as compared to injections or oral medications.
3) Sustained drug delivery.
4) A relatively rapid onset of action can be achieved relative to the oral route, and the formulation can be removed if therapy is required to be discontinued.
5) Increased ease of drug administration.
6) Though less permeable than the sublingual area, the buccal mucosa is well vascularized, and drugs can be rapidly absorbed into the venous system underneath the oral mucosa.
7) In comparison to TDDS, mucosal surfaces do not have a stratum corneum. Thus, the major barrier layer to transdermal drug delivery is not a factor in transmucosal routes of administration. 8) Transmucosal delivery occurs is less-variable between patients, resulting in lower intersubject variability as compared to transdermal patches.
9) The large contact surface of the oral cavity contributes to rapid and extensive drug absorption.

Disadvantages of buccal drug delivery system

1) Low permeability of the buccal membrane: specifically when compared to the sublingual membrane.
2) Smaller surface area. The total surface area of membranes of the oral cavity available for drug absorption is 170 cm2 of which ~50 cm^2 represents non-keratinized tissues, including the buccal membrane.
3) The continuous secretion of saliva (0.5–2 l/day) leads to subsequent dilution of the drug.
4) Swallowing of saliva can also potentially lead to the loss of dissolved or suspended drug and, ultimately, the involuntary removal of the dosage form.

These are some of the problems that are associated with buccal drug delivery.

Limitations of buccal drug administration

1) Drugs which are unstable at buccal pH cannot be administered.
2) Eating and drinking may become restricted.
3) There is an ever present possibility of the patient swallowing the dosage form.
4) Over hydration may leads to slippery surface and structural integrity of the formulation may get disrupted by this swelling and hydration of the bioadhesive polymers.
5) Drugs which irritate the mucosa or have a bitter or unpleasant taste or an obnoxious odor cannot be administered by this route.
6) Only drug with small dose requirement can be administered.
7) Only those drugs which are absorbed by passive diffusion can be administered by this route. 8) Drugs contained in the swallowed saliva follow the pre-oral and advantages of buccal route are lost.

MATERIALS

Piroxicam-Provided by SURA LABS, Dilsukhnagar, Hyderabad. Tragacanth-Zydus Cadila, Ahmedabad, Xanthan gum-Acurate Pharma, Tamarind Gum-Sd fine Chem.Ltd. Mumbai, MCC-Chemdie Corporation. Magnesium stearate-Chemdie Corporation.Talc-Sd fine Chem.Ltd. Mumbai, Saccharin sodium-Sd fine Chem.Ltd. Mumbai.

METHODOLOGY

Characterization of Piroxicam

Organoleptic properties

Take a small quantity of sample and spread it on the white paper and examine it visually for color, odour and texture.

Determination of Piroxicam Melting point

The melting point of Piroxicam was determined by capillary tube method according to the USP. A sufficient quantity of Piroxicam powder was introduced into the capillary tube to give a compact column of 4-6 mm in height. The tube was introduced in electrical melting point apparatus and the temperature was raised. The melting point was recorded, which is the temperature at which the last solid particle of Piroxicam in the tube passed into liquid phase**.**

Preformulation studies

Analytical method used in the determination of Piroxicam

Preparation of 0.2M NaOH Solution: Dissolved 4g of Sodium hydroxide pellets in to 1000mL of Purified water and mixed

Preparation of pH 6.8 Phosphate buffer: Dissolved 6.805 g of Potassium dihydrogen phosphate in to 800mL of purified water and mixed added 112mL of 0.2M NaOH solution and mixed. Diluted to volume 1000mL with purified water and mixed. Than adjusted the pH of this solution to 6.8 with 0.2M NaOH solution.

Preparation of pH 7.4 phosphate buffer: Accurately measured 250 mL of 0.2M potassium dihydrogen ortho phosphate and 195.5 mL of 0.2M NaOH was taken into the 1000 mL volumetric flask. Volume was made up to 1000 mL with distilled water.

Preparation of standard graph in phosphate buffer pH 6.8: 100 mg of Pure drug was dissolved in small amount of ethanol (5-10 ml), allowed to shake for few minutes and then the volume was made up to 100ml with phosphate buffer pH 6.8, from this primary stock (1mg/ml), 10 ml solution was transferred to another volumetric flask made up to 100 ml with phosphate buffer pH 6.8. From this secondary stock 0.5, 1, 1.5, 2, 2.5, ml was taken separately and made up to 10 ml with phosphate buffer pH 6.8 to produce 5, 10, 15, 20, 25 µg/ml respectively. The

absorbance was measured at 227 nm using a UV spectrophotometer. Standard calibration curve values were shown in Table (9.1). The standard calibration curve of Piroxicam in phosphate buffer pH 6.8 was shown.

Preparation of standard graph in phosphate buffer pH 7.4: 100 mg of drug was dissolved in small amount of ethanol and sonicated to dissolve and make the volume up to 100ml with phosphate buffer pH 7.4, from this primary stock(1mg/ml), 10 ml solution was transferred to another volumetric flask made up to 100 ml with phosphate buffer pH 7.4. From this secondary stock 0.5, 1, 1.5, 2, 2.5 ml were taken separately and made up to 10 ml with phosphate buffer pH 7.4, to produce 5, 10, 15, 20, 25 µg/ml respectively. The absorbance was measured at 230 nm using a UV spectrophotometer. Standard calibration curve values were shown in Table (9.2). The standard calibration curve of Piroxicam in phosphate buffer pH 7.4 was shown in fig 9.2.

Solubility Studies

The solubility of Piroxicam in phosphate buffer solution pH 6.8 was determined by phase equilibrium method. An excess amount of drug was taken into 20 ml vials containing 10 ml of phosphate buffers (pH 6.8). Vials were closed with rubber caps and constantly agitated at room temperature for 24 hr using rotary shaker. After 24 hr, the solution was filtered through 0.2µm Whattman's filter paper. The amount of drug solubilized was then estimated by measuring the absorbance at 227 nm using a UV spectrophotometer.

The standard curves for Piroxicam were established in phosphate buffers (pH 6.8) and from the slope of the straight line the solubility of Piroxicam was calculated. The studies were repeated in triplicate (n = 3), and mean was calculated.

Preparation of Tablets

Then the powder blend was compressed into tablets by the direct compression method using 6mm flat faced punches. The tablets were compressed using a sixteen station LAB PRESS rotary tablet-punching machine. The weight of the tablets was determined using a digital balance and thickness with digital screw gauge. Composition of the prepared bioadhesive buccal tablet formulations of Piroxicam were given in Table 8.4.

Table 1: Ingredienst categories

S.No	INGREDIENTS	USES
1.	Piroxicam	API
2.	Tragacanth	Polymer
3.	Xanthan gum	Polymer
4.	Tamarind Gum	Polymer
5.	MCC	Adsorbent; Suspending agent
6.	Magnesium stearate	Lubricant
7.	Talc	Anticaking agent
8.	Saccharin sodium	Artificial sweetener

Table 2: Formulation Chart

INGREDIENTS	FORMULATION CODES								
(MG)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Piroxicam	20	20	20	20	20	20	20	20	20
Tragacanth	10	20	30	-	-	-	-	-	-
Xanthan gum	-	-	-	10	20	30	-	-	-
Tamarind Gum	-	-	-	-	-	-	10	20	30
MCC	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Magnesium stearate	4	4	4	4	4	4	4	4	4
Talc	5	5	5	5	5	5	5	5	5
Saccharin sodium	10	10	10	10	10	10	10	10	10
Total weight	100	100	100	100	100	100	100	100	100

RESULTS AND DISCUSSION

Organoleptic properties

Table 3: Organoleptic properties

S NO.	Properties	Reported results	Observed results
1	State	Solid	Solid
2	Colour	White	White
3	Odour	Odourless	Odourless
4	Melting point	198-200°C	199.1°C

Solubility Studies

Table 4: Solubility studies

S.No	Medium	Amount present (µg/mL)
1	Phosphate pH 6.8 buffer	98.10
2	Phosphate pH 7.4 buffer	96.54

Saturation solubility of Piroxicam in various buffers were studied and shown in the Table 9.1. The results revealed that the solubility of the Piroxicam was increased from pH 6.8 to 7.4. The solubility of the Piroxicam in phosphate buffer pH 6.8 is 98.10µg/mL and it was selected as the suitable media for the release studies because the pH of the phosphate buffer pH 6.8 is nearer to that of buccal mucosa pH, Based on the Solubility study more solubility is showed in pH 6.8, So pH 6.8 is selected for Dissolution medium.

Standard graph in phosphate buffer pH 6.8 (λ_{max} 227 nm)

Standard graph of Piroxicam was plotted as per the procedure in experimental method and its linearity is shown in Table 9.2 and Fig 9.1**.** The standard graph of Piroxicam showed good linearity with R^2 of 0.999, which indicates that it obeys "Beer- Lamberts" law.

Table 5: Standard graph values of Piroxicam in pH 6.8 phosphate buffer

Concentration (µg/mL)	Absorbance
0	0
5	0.127
10	0.227
15	0.314
20	0.422
30	0.617

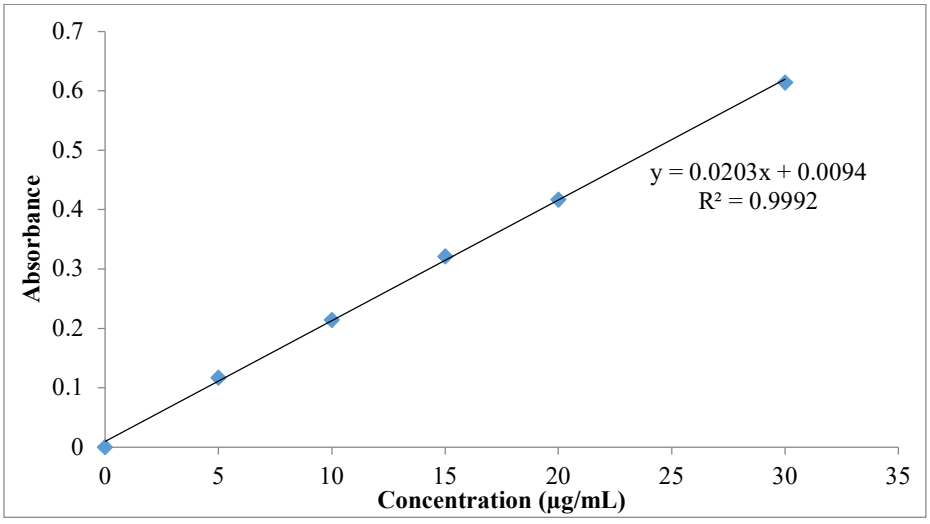

Fig 2: Standard graph of Piroxicam in pH 6.8 phosphate buffer

Standard graph in phosphate buffer pH 7.4 (λ_{max} 230 nm)

Standard graph of Piroxicam was plotted as per the procedure in experimental method and its linearity is shown in Table 9.3 and Fig 9.2. The standard graph of Piroxicam showed good linearity with R^2 of 0.999, which indicates that it obeys "Beer- Lamberts" law.

Table 6: Standard graph values of Piroxicam in pH 7.4 phosphate buffer

Concentration (µg/mL)	Absorbance
0	0
5	0.117
10	0.214
15	0.321
20	0.417
30	0.614

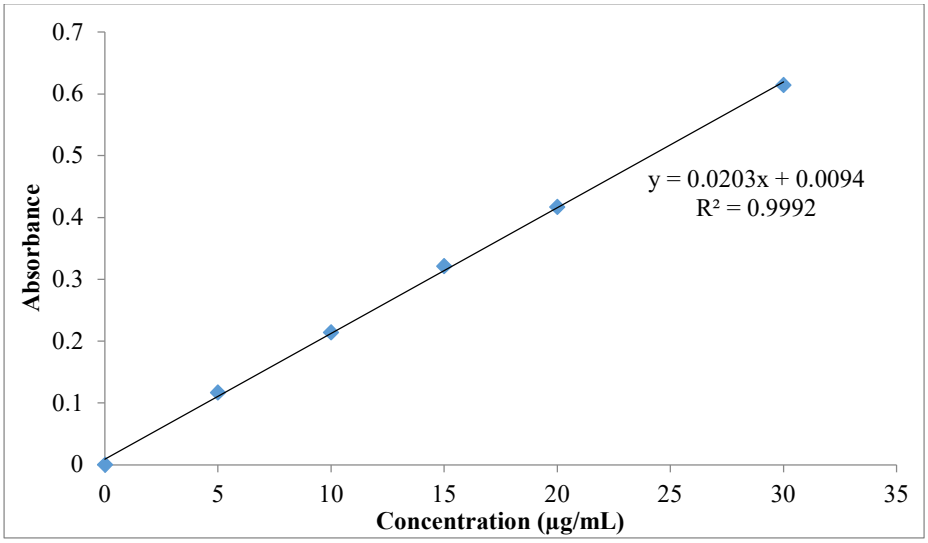

Fig 3: Standard graph of Piroxicam in pH 7.4 phosphate buffer

Evaluation

Characterization of pre-compression blend

Table 7: Physical properties of pre-compression blend

Formulation Code	Angle of repose (Ɵ)	Bulk density(gm/cm^3)	Tappeddensity (gm/cm^3)	Carr's Index (%)	Hausner's ratio
F1	24.72 ± 0.01	0.345 ± 0.018	0.401 ± 0.012	13.97 ± 0.01	1.16 ± 0.02
F2	19.66 ± 0.02	0.332 ± 0.002	0.375 ± 0.015	11.46 ± 0.01	1.13 ± 0.01
F3	20.16 ± 0.015	0.465 ± 0.015	0.532 ± 0.001	12.59 ± 0.01	1.14 ± 0.01
F4	21.41 ± 0.01	0.421 ± 0.002	0.492 ± 0.002	14.43 ± 0.02	1.17 ± 0.02
F5	20.60 ± 0.015	0.382 ± 0.001	0.439 ± 0.002	12.98 ± 0.01	1.15 ± 0.01
F6	20.36 ± 0.015	0.523 ± 0.002	0.604 ± 0.017	13.41 ± 0.02	1.15 ± 0.01
F7	19.98 ± 0.01	0.348 ±0.001	0.401 ± 0.001	13.22 ± 0.01	1.15 ± 0.01
F8	40.13 ± 0.01	0.412 ±0.015	0.530 ±0.021	22.23 ± 0.01	1.29 ± 0.01
F9	39.90 ± 0.01	0.424 ± 0.001	0.517 ± 0.01	18.00 ± 0.01	1.21 ± 0.01

All the values represent n=3

Tablet powder blend was subjected to various preformulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range showing that the powder has good flow properties. The tapped density of all the formulations powders has good flow properties. The compressibility index of all the formulations was found to be 11.46 to 22.23 which

show that the powder has good flow properties. All the formulations have shown the hausner ratio 1.13 to 1.29 indicating the powder has good flow properties.

Evaluation of buccal tablets

Physical evaluation of Piroxicam buccal tablets

The results of the weight variation, hardness, thickness, friability and drug content of the tablets are given in Table 9.5. All the tablets of different batches complied with the official requirement of weight variation as their weight variation passes the limits. The hardness of the tablets ranged from 3.0 to 4.6 kg/cm^2 and the friability values were less than 0.61 % indicating that the buccal tablets were compact and hard. The thickness of the tablets ranged from 1.01 – 1.92 mm. All the formulations satisfied the content of the drug as they contained 97.87-100.02 % of Piroxicam. Thus all the physical attributes of the prepared tablets were found to be practically within control limits.

Table 8: Physical evaluation of Piroxicam buccal tablets

Formulation code	Weight variation (mg)	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Content uniformity (%)
F1	98.47	1.01	3.9	0.54	98.24
F2	96.92	1.92	3.0	0.42	99.46
F3	99.30	1.35	4.3	0.36	100.02
F4	97.12	1.87	3.1	0.61	97.64
F5	100.12	1.28	4.2	0.50	98.99
F6	99.27	1.13	4.6	0.46	99.06
F7	100.04	1.79	3.1	0.40	98.42
F8	100.25	1.35	4.0	0.37	97.87
F9	97.80	1.60	3.8	0.29	98.31

***In vitro* release studies**

In vitro drug release studies were conducted in phosphate buffer pH 6.8 and the studies revealed that the release of Piroxicam from different formulations varies with characteristics and composition of matrix forming polymers as shown in graphs 9.3 to 9.5.

Table 9: *In vitro* dissolution data for formulations F1 – F9

TIME (H)	CUMULATIVE PERCENTE OF DRUG RELEASE								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	21.59	17.19	20.14	31.06	25.39	20.92	18.82	15.10	11.58
1	26.34	36.30	23.39	38.26	31.19	28.03	22.09	17.49	20.16
2	37.20	45.11	30.92	46.17	37.24	32.51	31.99	27.60	26.09
3	52.87	62.24	35.57	50.96	46.08	40.99	38.46	35.18	34.10
4	68.46	69.97	44.26	56.32	57.77	45.42	50.06	44.82	53.23
5	79.22	74.43	56.41	68.24	64.69	54.60	56.33	53.99	57.42
6	86.97	81.19	62.14	74.12	71.53	60.17	78.10	65.76	65.99
7	97.17	87.13	74.06	89.03	76.11	77.96	86.71	78.14	76.37
8		91.06	87.79	99.61	90.72	85.12	94.13	88.34	81.83

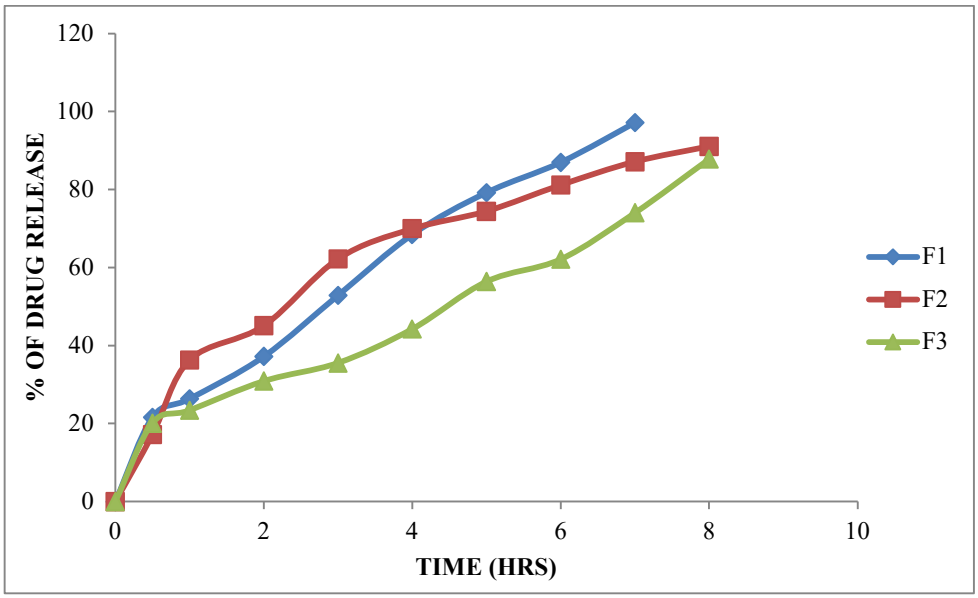

Fig 4: *In vitro* dissolution data for formulations F1 – F3 by using Tragacanth polymer

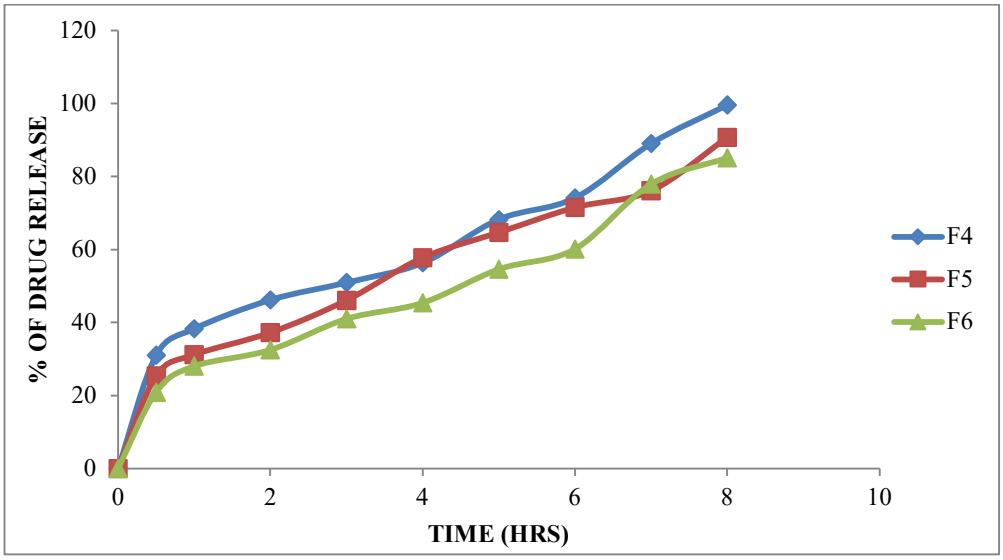

Fig 5: *In vitro* dissolution data for formulations F4 –F6 by using Xanthan gum polymer

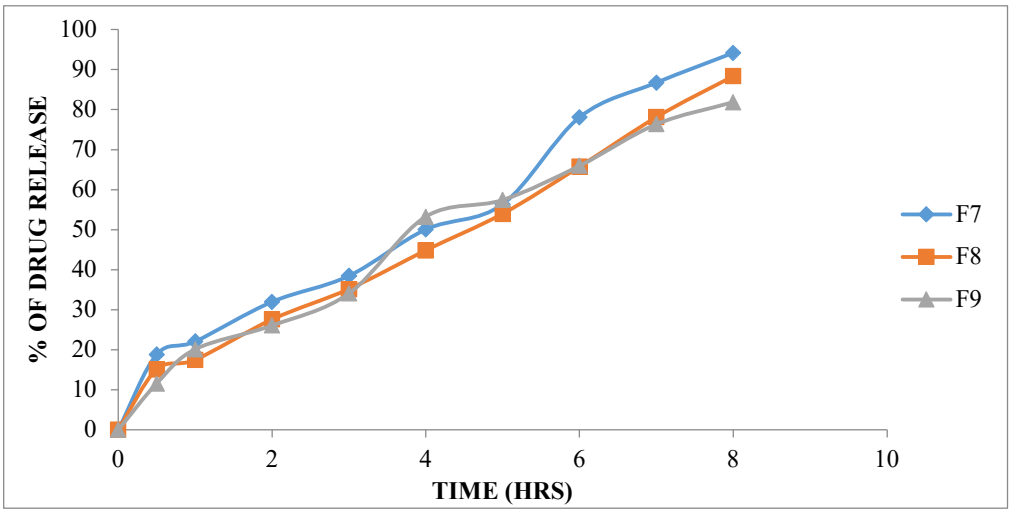

Fig 6: *In vitro* dissolution data for formulations F7- F9 by using Tamarind Gum polymer

From the above graphs it was evident that Tragacanth in the concentration of 20mg of polymer of the total tablet weight (F2) drug with other Two Formulations F1, F3. Where as in F2 formulation the quantity of polymer was less hence it showed more drug retardation with more drug release that is 91.06 % in 8 hrs. From the above graphs it was evident that Xanthan gum in the Polymer concentration of 5mg (F4) is showing better result 99.61% drug release when compared with other two formulations F5, F6, as the concentration of polymer increases the retarding of drug release decreased.

From the above graphs it was evident that Tamarind Gum in the Polymer concentration 10mg formulation (F7) is showing better result 94.13% drug release when compared with other two formulations. Where as in F8, F9 formulations the concentration become high and the drug release was less.

From the above results it was evident that the formulation F4 is best formulation with desired drug release pattern extended up to 8 hours.

Based on the Dissolution data F2, F4 and F7 was observed more drug release compared to other formulation, So F2, F4 and F7 formulation was selected pH study.

Table 10: Moisture absorption, surface pH of selected formulations

Formulation Code	Moisture absorption	Surface pH
F2	83	5.82
F4	97	5.05
F7	92	6.10

The moisture absorption studies give important information of the relative moisture absorption capacities of polymers and it also give information regarding whether the formulations maintain the integrity or not. Among the selected formulations F4 formulation shown good moisture absorption.

The surface pH of the buccal tablets was determined in order to investigate the possibility of any side effects. As an acidic or alkaline pH may cause irritation to the buccal mucosa, it was determined to keep the surface pH as close to neutral as possible. The surface pH of the selected formulations was found to be 5.05 to 6.10 and the pH was near to the neutral. These results suggested that the polymeric blend identified was suitable for oral application and formulations were not irritant to the buccal mucosa.

Based on the pH data F4 Formulation was observed lower side, Hence F4 Formulation was considered as Optimized Formulation.

Release kinetics

Out of all the prepared formulation, F4 was selected as optimized formulation as it gave the best results for cumulative percentage drug release.

Data of *in vitro* release studies of formulations which were showing better drug release were fit into different equations to explain the release kinetics of Piroxicam release from buccal tablets. The data was fitted

into various kinetic models such as zero, first order kinetics; higuchi and korsmeyer peppas mechanisms and the results were shown in below table.

Table 11: Release kinetics and correlation coefficients (R^2)

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	LOG(%) RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE / t)	1/CUM% RELEASE	PEPPAS log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3-Qt1/3
0	0	0			2.000				100	4.642	4.642	0.000
31.06	0.5	0.707	1.492	-0.301	1.838	62.120	0.0322	-0.508	68.94	4.642	4.100	0.541
38.26	1	1.000	1.583	0.000	1.791	38.260	0.0261	-0.417	61.74	4.642	3.952	0.689
46.17	2	1.414	1.664	0.301	1.731	23.085	0.0217	-0.336	53.83	4.642	3.776	0.866
50.96	3	1.732	1.707	0.477	1.691	16.987	0.0196	-0.293	49.04	4.642	3.660	0.981
56.32	4	2.000	1.751	0.602	1.640	14.080	0.0178	-0.249	43.68	4.642	3.522	1.120
68.24	5	2.236	1.834	0.699	1.502	13.648	0.0147	-0.166	31.76	4.642	3.167	1.475
74.12	6	2.449	1.870	0.778	1.413	12.353	0.0135	-0.130	25.88	4.642	2.958	1.684
89.03	7	2.646	1.950	0.845	1.040	12.719	0.0112	-0.050	10.97	4.642	2.222	2.420
99.61	8	2.828	1.998	0.903	-0.409	12.451	0.0100	-0.002	0.39	4.642	0.731	3.911

Drug – excipients compatibility studies by physical observation

Piroxicam was mixed with various proportions of excipients showed no color change at the end of two months, proving no drug-excipient interactions.

FTIR

FTIR spectra of the drug and the optimized formulation were recorded. The FTIR spectra of pure Piroxicam drug, drug with polymers (1:1) shown in the below figures respectively. The major peaks which are present in pure drug Piroxicam are also present in the physical mixture, which indicates that there is no interaction between drug and the polymers, which confirms the stability of the drug.

There was no disappearance of any characteristics peak in the FTIR spectrum of drug and the polymers used. This shows that there is no chemical interaction between the drug and the polymers used. The presence of peaks at the expected range confirms that the materials taken for the study are genuine and there were no possible interactions.

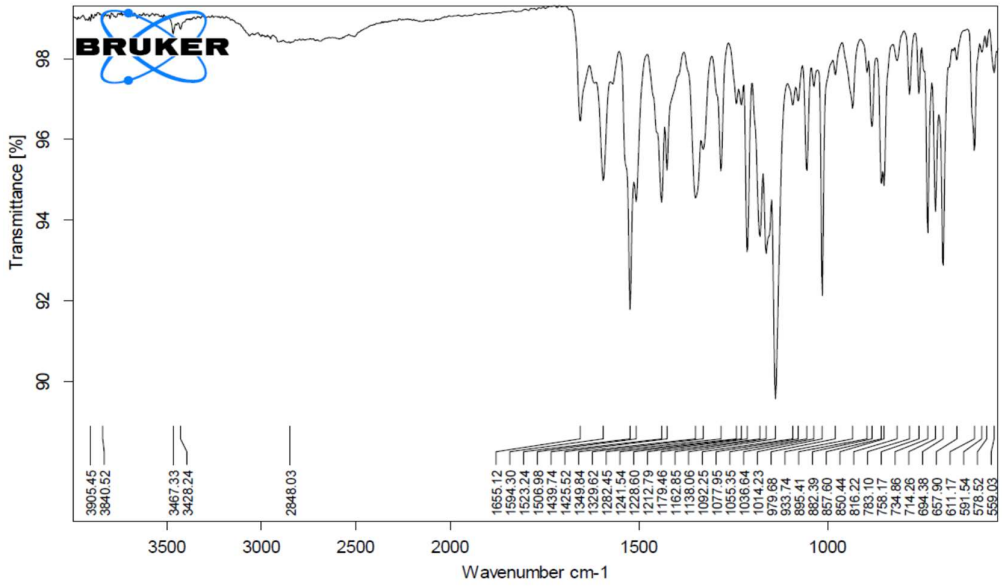

Fig 7: FTIR Peak of pure drug Piroxicam

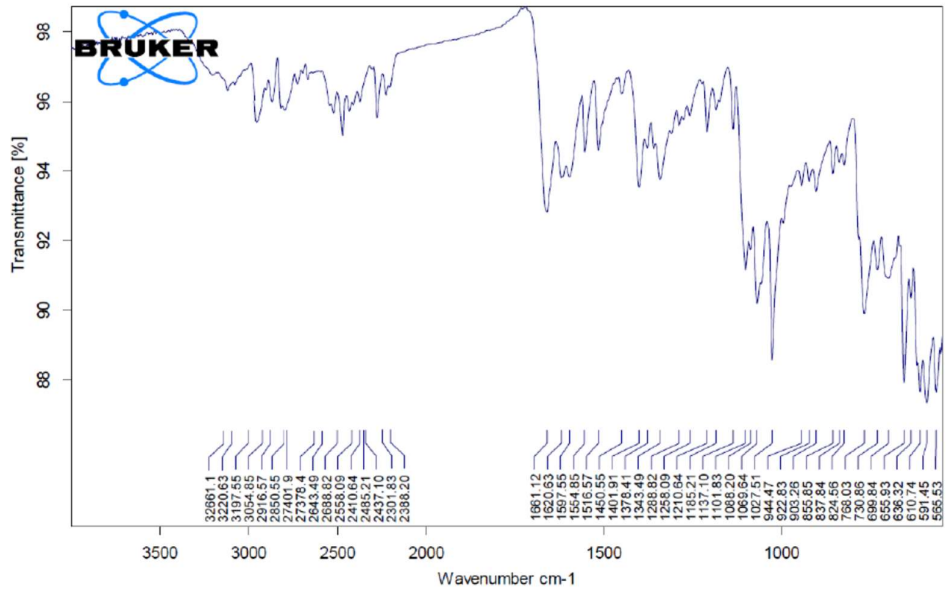

Fig 8: FTIR Peak of Optimised formulation

Table 12: FTIR studies of Piroxicam with superdisintegrants

IR spectra	Peak of functional groups [Wave length (cm-1)]			
	N-H stretch	C-H stretch	C=C stretch	OH bend
Standard spectra	3339.028	2933.879	1529.315	939.582
Piroxicam	3428.24	2848.03	1594.30	979.68
Piroxicam + superdisintegrants	3220.63	2850.22	1554.85	944.47

SUMMARY

The Piroxicam is nonsteroidal anti-inflammatory drug (NSAID) which is used in treatment of relieve the symptoms of painful inflammatory conditions like arthritis. The aim of this work was to develop a mucoadhesive buccal tablet for the buccal delivery of the Piroxicam via buccal mucosa. In the present work, an attempt was

made to design efficacious and prolonged release mucoadhesive buccal tablets of Piroxicam using various polymers to reduce dosing frequency, decrease gastric irritation and to improve patient compliance. Total 9 formulations of Piroxicam mucoadhesive buccal tablets are designed to release drug at mucosal site in unidirectional pattern for extended period of time without wash out of drug by saliva. Tragacanth, Xanthan gum and Tamarind Gum were selected as mucoadhesive polymer. UV Spectroscopic method was used for the determination of Piroxicam in pH 6.8 and pH 7.4 medium at 227 nm. The results of the drug–excipient compatibility FT-IR studies revealed that there was no chemical interaction between the pure drug and excipients. The tablets were prepared by direct compression method. 9 formulations were designed by using central composite design using different concentrations of Tragacanth, Xanthan gum and Tamarind Gum.The prepared formulations were evaluated for the Precompression parameters such as angle of repose, bulk density, and % compressibility. All the parameters were found to be within the limits. The post compression parameters such as weight variation, thickness, hardness, friability, drug content, surface pH, Moisture absorption and *In-vitro* dissolution.

From the data obtained, it is observed that Amongst the various polymers used in the study, the buccal tablets were formulated by direct compression method using Xanthan gum (10 mg) exhibited better results than compared to those other combination of polymers in different concentration. The effectiveness of polymers (Xanthan gum) on the drug release was explained.

CONCLUSION

The present research was carried out to develop mucoadhesive buccal tablets of Piroxicam using various polymers. The preparation process was simple, reliable and inexpensive. All the prepared tablet formulations were found to be good without capping and chipping. The mucoadhesive buccal tablets of Piroxicam could be prepared using Tragacanth, Xanthan gum and Tamarind Gum polymers by using direct compression method. The prepared mucoadhesive buccal tablets subjected to infrared spectrum study suggested that there was no drug - polymer interaction. All the prepared tablets were in acceptable range of weight variation, hardness, thickness, friability and drug content as per pharmacopoeial specification. The surface pH of prepared buccal tablets was in the range of salivary pH, suggested that prepared tablets could be used without risk of mucosal irritation. The *in-vitro* release of Piroxicam was extended for 8h. Formulations F4 batch shows good *in vitro* drug release 99.61%. From the results of present investigation it can be concluded that Piroxicam can certainly be administered through the oral mucosa and Xanthan gum is suitable for development of Buccoadhesive system.

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